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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,627	06/19/2006	Heinz Von Der Kammer	37998-237368	8551

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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	PAPER NUMBER
1632	
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07/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,627	VON DER KAMMER ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *1-10,13-24,27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,12,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4-9-07&7-17-08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-28 remain pending.

Election/Restrictions

Applicant's election without traverse of Group VII, claims 11, 12, 25 and 26, in the reply filed on 6-11-08 is acknowledged.

Claims 1-10, 13-24, 27 and 28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6-11-08.

Specification

This application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because there are sequences throughout the specification without SEQ ID NOs. Applicants must file a "Sequence Listing" accompanied by directions to enter the listing into the specification as an amendment. Applicant also must provide statements regarding sameness and new matter with regards to the CRF and the "Sequence Listing." Failure to fully comply with the sequence rules in response to the instant office action will be considered non-responsive.

Claim Rejections - 35 USC § 112

Claims 11, 12, 25 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in

the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed toward a method of screening for a modulator of neurodegenerative disease or related diseases or disorders. The claims encompass screening for modulators that increase neurodegenerative diseases or disorders, which does not have a disclosed, enabled use. The claims should be limited to screening for compounds that decrease neurodegenerative diseases or disorders.

The claims are directed toward screening for compounds that modulate neurodegenerative disease by administering a compound to a test animal that is predisposed to developing or has already developed symptoms of neurodegenerative disease in respect to i) a gene coding for HIF3a, ii) a transcription product of a gene coding for HIF3a, iii) a translation product of a gene coding for HIF3a, and iv) a fragment, derivate or variant of i), ii) or iii). The specification and the art at the time of filing do not teach any neurodegenerative disease that correlates to i) a gene coding for HIF3a, ii) a transcription product of a gene coding for HIF3a, iii) a translation product of a gene coding for HIF3a, and iv) a fragment, derivate or variant of i), ii) or iii). In particular, the specification and the art at the time of filing do not teach any animal models having a neurodegenerative disease that relates to i)-iv) as claimed. While Alzheimer's disease (AD) models were known in the art (pg 25, lines 15-24), the specification does not provide adequate guidance that known animal models of AD have "symptoms of neurodegenerative diseases or related diseases or disorders in respect of the substances recited in i)-iv)" as claimed. I.e. the specification does not

teach the models correlate to wild-type, overexpression, deletion or mutation of HIF3a as encompassed by the claims. The specification does not provide any reason to believe that all models of AD correlate to HIF3a. Accordingly, it would have required those of skill undue experimentation to determine which neurodegenerative diseases are affected by i) a gene coding for HIF3a, ii) a transcription product of a gene coding for HIF3a, iii) a translation product of a gene coding for HIF3a, and iv) a fragment, derivate or variant of i), ii) or iii) as broadly claimed.

The claims are directed toward screening for compounds that modulate neurodegenerative disease by

a) administering a compound to a test animal that is predisposed to developing or has already developed symptoms of neurodegenerative disease in respect to i) a gene coding for HIF3a, ii) a transcription product of a gene coding for HIF3a, iii) a translation product of a gene coding for HIF3a, and iv) a fragment, derivate or variant of i), ii) or iii);

b) measuring the activity and/or level of i) a gene coding for HIF3a, ii) a transcription product of a gene coding for HIF3a, iii) a translation product of a gene coding for HIF3a, and iv) a fragment, derivate or variant of i), ii) or iii);

c) measuring the activity and/or level of i)-iv) in a control animal that is predisposed to developing or has already developed symptoms of neurodegenerative disease in respect to i)-iv) to which no test compound has not been administered; and

d) comparing the activity and/or level of i)-iv) in the animals, wherein a change in the activity and/or level of i)-iv) indicates the test compound is a modulator of said neurodegenerative disease.

The specification and the art at the time of filing do not teach any animal models that overexpress HIF3a, that have a mutant HIF3a or that have a deletion in HIF3a. To date, no experiments have been described that demonstrate a relationship between dysregulation of HIF3a gene expression and the pathology of neurodegenerative diseases, in particular AD [Alzheimer's Disease]. Likewise, no mutations in the HIF3a gene have been described to be associated with said diseases." (pg 12, lines 1-6). Given the lack of guidance how to make or find such models, it would require those of ordinary skill undue experimentation to make or find such models needed for the methods claimed.

Since the time of filing, Yamashita (Mol. Cell. Biol. Feb. 2008, Vol. 28, No. 4, pg 1285-1297) taught HIF3a knockout mice had enlarged right ventricles and impaired lung remodeling. The structure of the mice is encompassed by the structure of test animals in step a) of claim 11; the mice of Yamashita may fit the functional language in step a) as well because they may be predisposed to neurodegenerative disease. However, Yamashita did not teach they were a model of neurodegenerative disease. The specification does not teach HIF3a knockout mice have a phenotype that correlates to neurodegenerative disease. Therefore, the claims should not encompass using HIF3a knockout mice to screen for modulators of neurodegenerative disease.

The specification describes making transgenic drosophila melanogaster expressing human BACE and HIF3a using the method of Greeve (pg 57, (xii)). The disclosure is not enabling because it does not set for the structure of the construct used to make the files, that the transgenic flies had a neurodegenerative disease, or that the transgenic flies had a neurodegenerative disease that correlated to HIF3a overexpression in humans with neurodegenerative disease. The specification does not provide adequate guidance that the transgenic flies model neurodegenerative disease in humans. The specification teaches transgenic flies with HIF3a under the control of the eye specific gmr-GAL4 (pg 59, line 16). The specification does not teach how those flies model neurodegenerative disease as claimed. Without such guidance, it would have required those of skill undue experimentation to determine how to make and use the transgenic flies described in the specification in the methods now claimed.

The specification does not enable screening for modulators of SEQ ID NO: 4 (claim 26) using any test animal predisposed to or having a neurodegenerative disease as claimed. The specification does not teach how to use any test animal having symptoms of Alzheimer's disease (AD), for example, to screen for modulators of SEQ ID NO: 4. Nor is such a method readily apparent from the art at the time of filing. If the test animal overexpresses amyloid precursor protein (APP) and has symptoms of AD, for example, it cannot be determined how to use the mice to screen for modulators of SEQ ID NO: 4. Without such guidance, those of skill would be on their own to determine how to screen for modulators of SEQ ID NO: 4 using any test animal having

symptoms of neurodegenerative disease, which is not considered an enabling disclosure. Clarification is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11, 12, 25 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is indefinite because the phrase "screening for a modulator of neurodegenerative diseases, or related diseases or disorders of one or more substances selected from the group consisting of i) a gene coding for HIF3a, ii) a transcription product of a gene coding for HIF3a, iii) a translation product of a gene coding for HIF3a, and iv) a fragment, derivate or variant of i), ii) or iii)." It is unclear how the neurodegenerative diseases can be "of" i) a gene coding a gene coding for HIF3a, ii) a transcription product of a gene coding for HIF3a, iii) a translation product of a gene coding for HIF3a, and iv) a fragment, derivate or variant of i), ii) or iii). In other words, it is unclear how the neurodegenerative diseases must correlate to HIF3a. Clarification is required.

Likewise, claim 11 is indefinite because the phrase "a test animal which is predisposed to developing or has already developed symptoms of a neurodegenerative disease or related diseases or disorders in respect of the substances selected from the group consisting of i) a gene coding for HIF3a, ii) a transcription product of a gene

coding for HIF3a, iii) a translation product of a gene coding for HIF3a, and iv) a fragment, derivate or variant of i), ii) or iii)." It is unclear how the neurodegenerative diseases can be "in respect of" the substance of i)-iv). In other words, it is unclear how the neurodegenerative diseases of the test animal correlates to HIF3a. Clarification is required.

The metes and bounds of what applicants consider diseases "related" to neurodegenerative diseases cannot be determined (claim 11, preamble and step a)). Such diseases are not defined in the specification and are not readily apparent from the art at the time of filing. Is cardiovascular disease related to any neurodegenerative disease? If so, it is unclear if is any cardiovascular disease encompassed by the claim or if the cardiovascular disease must meet certain criteria.

Step c of claim 11 does not make sense because it does not ensure the control and test animals have the same predisposition to developing or have the same neurodegenerative disease. Without such a limitation the method does not make sense.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 11 is rejected under 35 U.S.C. 102(a) as being anticipated by Heidbreder (FASEB, Aug. 2003, Vol. 17, pg 1541-1543).

Heidbreder administered half of normal O_2 tensions to male Wistar rats (pg 1541, col. 1, last two lines) and measured HIF3a levels, which is equivalent to steps a and b. Half of normal O_2 tension levels is a “test compound." The rats are test animals “predisposed to developing" or have "already developed symptoms of neurodegenerative disease or related diseases or disorders in respect of the substances recited in (i) to (iv)” because the metes and bounds of animals encompassed by the phrase are unclear (see the second and third 112/2nd rejections above). The HIF3a levels were compared to controls, which is equivalent to step c).

Claim 11 is rejected under 35 U.S.C. 102(a) as being anticipated by Makino (J. Biological Chem., Sept. 6, 2002, Vol. 277, No. 36, pg 32405-32408).

Makino exposed mice to hypoxia (6% O_2 – pg 32407, col. 2, line 22) and normal mice, measured HIF3a levels in various tissues and compared (Fig. 3), which is equivalent to steps a, b and c. 6% O_2 is a “test compound." The mice are test animals “predisposed to developing" or have "already developed symptoms of neurodegenerative disease or related diseases or disorders in respect of the substances recited in (i) to (iv)” because the metes and bounds of animals encompassed by the phrase are unclear (see the second and third 112/2nd rejections above).

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Bazan (Mol. Neurobiology, 2002, Vol. 2-3, pg 283-298).

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Patent Examiner